Annual Surveillance Summary: *Escherichia coli (E. coli)* Infections in the Military Health System (MHS), 2016

NMCPHC-EDC-TR-407-2017

By Kristen Rossi and Uzo Chukwuma
EpiData Center Department
Prepared June 2017

REPORT DOCUMENTATION PAGE		*Form Approved* *OMB No. 0704-0188*

The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden, to the Department of Defense, Executive Service Directorate (0704-0188). Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.
PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ORGANIZATION.

1. REPORT DATE *(DD-MM-YYYY)* June 2017	2. REPORT TYPE Technical Report	3. DATES COVERED *(From - To)* 01 January 2016 - 31 December 2016

4. TITLE AND SUBTITLE Annual Surveillance Summary: Escherichia coli (E. coli) Infections in the Military Health System (MHS), 2016	5a. CONTRACT NUMBER
	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Kristen Rossi, Uzo Chukwuma	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) EpiData Center Navy and Marine Corps Public Health Center 620 John Paul Jones Circle, Suite 1100 Portsmouth, VA 23708-2103	8. PERFORMING ORGANIZATION REPORT NUMBER NMCPHC-EDC-TR-407-2017
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) EpiData Center Navy and Marine Corps Public Health Center 620 John Paul Jones Circle, Suite 1100 Portsmouth, VA 23708-2103	10. SPONSOR/MONITOR'S ACRONYM(S) EDC, NMCPHC
	11. SPONSOR/MONITOR'S REPORT NUMBER(S) NMCPHC-EDC-TR-407-2017

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The EpiData Center Department (EDC) conducts routine surveillance of Escherichia coli (E. coli) incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for E. coli in calendar year (CY) 2016. The E. coli incidence rate among MHS beneficiaries demonstrated a minimal increase of 3.1% during 2016 in relation to the weighted historic incidence rate. Characteristics of E. coli infections are concurrent with existing literature, and occurred at higher rates among females, manifested most commonly as urinary tract infections (UTIs), and primarily identified as community-associated (CA) cases. Approximately 21% of all prevalent E. coli infections during 2016 were multidrug-resistant, underscoring the need for continued surveillance. Viable treatment options are available for E. coli infections in the MHS, but some commonly prescribed antibiotics no longer display sufficient efficacy or are no longer recommended for treating select conditions.

15. SUBJECT TERMS
Health Level 7 (HL7), microbiology, surveillance, Escherichia coli, multidrug resistance (MDR), carbapenem-resistant Enterobacteriaceae (CRE), healthcare-associated infections (HAIs)

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON Uzo Chukwuma MPH
a. REPORT	b. ABSTRACT	c. THIS PAGE			
U	U	U	UU	19	19b. TELEPHONE NUMBER *(Include area code)* 757-953-0970

Reset

Standard Form 298 (Rev. 8/98)
Prescribed by ANSI Std. Z39.18
Adobe Professional 7.0

NAVY AND MARINE CORPS PUBLIC HEALTH CENTER
PREVENTION AND PROTECTION START HERE

Abstract

The EpiData Center Department (EDC) conducts routine surveillance of *Escherichia coli (E. coli)* incidence and prevalence among all beneficiaries seeking care within the Military Health System (MHS). This report describes demographics, clinical characteristics, prescription practices, and antibiotic resistance patterns observed for *E. coli* in calendar year (CY) 2016.

Multiple data sources were linked to assess descriptive and clinical factors related to *E. coli*. Health Level 7 (HL7)-formatted Composite Health Care System (CHCS) microbiology data identified *E. coli* infections. These infections were matched to HL7-formatted CHCS pharmacy data to assess prescription practices, the Standard Inpatient Data Record (SIDR) to determine healthcare-associated exposures, Defense Manpower Data Center (DMDC) rosters to determine burden among Department of Defense (DOD) active duty (AD) service members, and the DMDC Contingency Tracking System (CTS) to determine Department of the Navy (DON) deployment-related infections.

The *E. coli* incidence rate among MHS beneficiaries demonstrated a minimal increase of 3.1% during 2016 (676.7 per 100,000 persons) in relation to the weighted historic incidence rate (656.2 per 100,000 persons per year). Characteristics of *E. coli* infections are concurrent with existing literature, and occurred at higher rates among females, manifested most commonly as urinary tract infections (UTIs), and primarily identified as community-associated (CA) cases. Approximately 21% of all prevalent *E. coli* infections during 2016 were multidrug-resistant, underscoring the need for continued surveillance. While antibiotic susceptibilities indicate that viable treatment options are available for *E. coli* infections in the MHS, some commonly prescribed antibiotics no longer display sufficient efficacy or are no longer recommended for treating select conditions. Further surveillance and analysis are warranted.

Contents

Background, Methods, and Limitations

The EpiData Center (EDC) at the Navy and Marine Corps Public Health Center (NMCPHC) prepares a retrospective report each calendar year (CY) that summarizes the demographics, clinical characteristics, prescription practices, and antibiotic susceptibility patterns for *Escherichia coli (E. coli)* infections among Military Health System (MHS) beneficiaries.

Literature review did not provide any new developments or research for *E. coli* infections. Additionally, no new methods or limitations were applied to this annual summary. As such, this report presents analytical results and discussion of CY 2016 data for *E. coli* infections in the MHS. The background, methods, and limitations relevant to this analysis have been discussed in a previous report (CY 2015 annual report for *E. coli*[1]).

The EDC also monitors other multidrug-resistant organisms (MDROs) of interest in the MHS.[2,3]

Results

Section A – Descriptive Epidemiology
Incidence of *Escherichia coli*

In 2016, the annual incidence rate (IR) for *E. coli* infection among MHS beneficiaries treated at a military treatment facility (MTF) was 676.7 per 100,000 persons per year. This reflects a 3.1% change above the weighted historic IR (656.2 per 100,000 persons per year). With the exception of the Marine Corps, incidence rates among MHS beneficiaries in the other services and the Department of Defense (DOD) active duty (AD) population increased above the weighted historic IR; however, all of the 2016 rates remained within two standard deviations of the weighted historic IR. Marine Corps MHS beneficiaries demonstrated a minor decrease in relation to the weighted historic IR, by less than one percent (Table 1).

Table 1. Incidence Rate (IR) for *Escherichia coli* Infections in the MHS, CY 2016

Population	2016 IR	Weighted Historic[a] IR 2013 - 2015	Two Standard Deviations: Weighted Historic[a] IR	2016	
				Direction	Percent Change[b]
MHS Beneficiaries	676.7	656.2	137.6	↑	3.1%
Air Force	616.4	608.6	132.3	↑	1.3%
Army	713.1	684.1	145.3	↑	4.2%
Marine Corps	699.2	702.2	150.8	↓	0.4%
Navy	646.7	616.2	120.8	↑	4.9%
DOD Active Duty	862.4	806.6	168.7	↑	6.9%

Rates are presented as the rate per 100,000 persons per year.
A green arrow indicates an increasing percent change and a blue arrow indicates a decreasing percent change.
[a] Historic IR reflects the weighted average of the three years prior to the analysis year.
[b] This reflects the percent change from the weighted historic IR to the IR of the current analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Demographic Distribution of *Escherichia coli*

In 2016, there were 63,672 incident *E. coli* infections identified among all MHS beneficiaries treated at an MTF. Incidence among females was nearly 11 times higher than among males. Beneficiaries aged 18-24 years experienced the highest incidence rate (1,151.9 per 100,000 persons per year) among all age groups, followed closely by beneficiaries 25-34 years old (1,126.3 per 100,000 persons per year). Among beneficiary types, AD service members had the highest incidence rate (862.4 per 100,000 persons per year), followed closely by family members (816.6 per 100,000 persons per year) (Table 2).

Table 2. Demographic Characteristics of *Escherichia coli* Infections in the MHS, CY 2016

	N = 63,672	
	Count	Rate
Gender[a]		
Female	58,060	1,258.3
Male	5,611	117.0
Age Group (in Years)		
0-17	6,309	322.3
18-24	13,178	1,151.9
25-34	13,526	1,126.3
35-44	8,388	1,004.0
45-64	14,163	689.8
65+	8,108	365.6
Beneficiary Type		
Active Duty	11,774	862.4
Family Members	44,696	816.6
Retired	4,092	187.2
Other[b]	3,110	--

[a] Gender was unable to be classified in one record.
[b] Rate is not reported due to variation in population denominator.
Rates are presented as the rate per 100,000 persons per year.
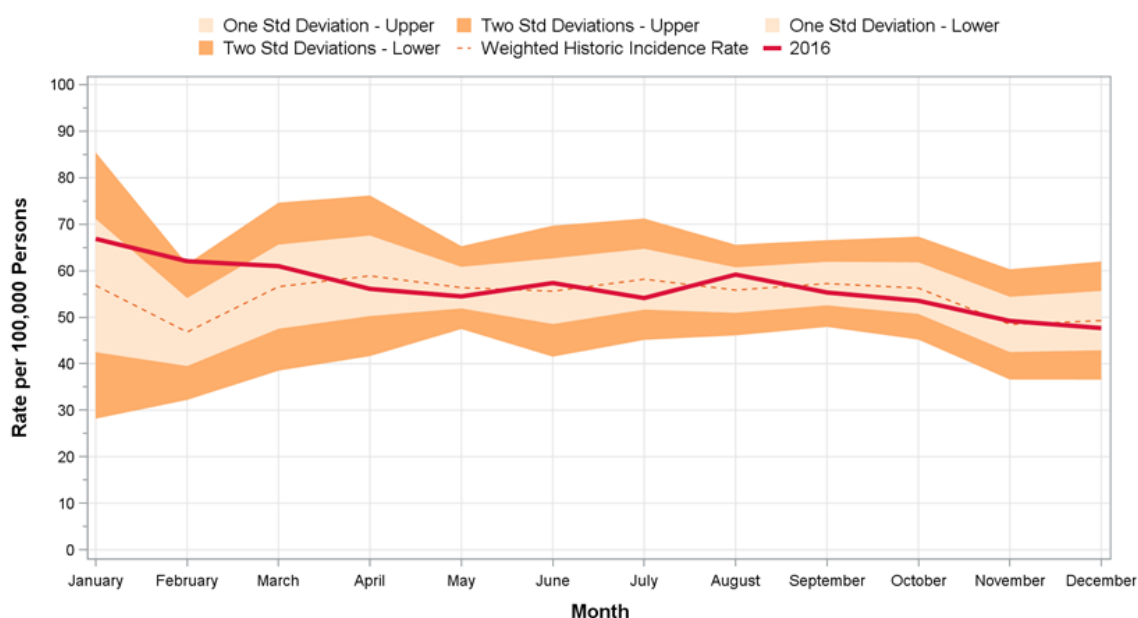Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Seasonality

Monthly incidence rates of *E. coli* infections in 2016 exceeded the weighted historic IR for six months of the year (January, February, March, June, August, and November). Incidence rates were highest in January and February, and exceeded two standard deviations above the weighted historic IR in February 2016. Monthly incidence rates from March through December remained within one standard deviation above or below the weighted historic IR, and were therefore consistent with prior historical observation (Figure 1). A downward trend in monthly incidence rates was demonstrated between August and December, with the lowest rates occurring in November and December.

Figure 1. Monthly Incidence of *Escherichia coli* Infections and Weighted Historic Incidence Rate (IR) Comparisons in the MHS, CY 2016

Rates are presented as the rate per 100,000 persons per year.
Bands indicate one and two standard deviations above and below the weighted historic monthly incidence rates (IR).
The weighted historic monthly IR is a weighted average of the three years prior to the analysis year.
Data Source: NMCPHC HL7-formatted CHCS microbiology and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Escherichia coli Clinical Characteristics

There were 65,535 prevalent *E. coli* infections identified among all MHS beneficiaries treated at an MTF in 2016. The majority of *E. coli* specimens were collected in the outpatient setting (97.5%) as non-invasive infections (99.2%) from urine samples (96.4%) (Table 3).

Table 3. Clinical Characteristics of *Escherichia coli* Prevalent Infections in the MHS, CY 2016

	N = 65,535	
	Count	Percentage
Specimen Collection Location		
Inpatient	1,637	2.5
Outpatient	63,898	97.5
Infection Type		
Invasive	506	0.8
Non-Invasive	65,029	99.2
Body Collection Site		
Blood	381	0.6
Respiratory	171	0.3
SSTI/Wound	1,009	1.5
Urine	63,194	96.4
Other	780	1.2

Data Source: NMCPHC HL7-formatted CHCS microbiology database.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Exposure Burden Metrics

Table 4 presents two different metrics describing the burden of MDRO infection rates for healthcare-associated exposures. In 2016, there were 239,946 direct care inpatient admissions across all MHS MTFs. The overall MDRO prevalence rate for *E. coli* was 11.2 per 1,000 inpatient admissions; this metric measures the exposure of infection at any point during the admission or one year prior. Within the United States (US), the Midwest region had the highest overall MDRO prevalence rate (15.4 per 1,000 inpatient admissions) and the South Atlantic had the lowest rate (8.9 per 1,000 inpatient admissions). The admission MDRO prevalence rate for *E.coli* was 10.6 per 1,000 inpatient admissions; this metric measures the magnitude of infection at the time of admission (importation of MDRO into the healthcare system) or one year prior. As with overall MDRO prevalence, within the US, the Midwest region had the highest admission MDRO prevalence rate (15.1 per 1,000 inpatient admissions) and the South Atlantic region had the lowest rate (8.3 per 1,000 inpatient admissions). Comparison of these two metrics suggests that the majority of *E. coli* infections were imported into the hospital setting from the community, as the overall MDRO prevalence rate was only slightly higher than the admission MDRO prevalence rate (11.2 vs. 10.6 per 1,000 inpatient admissions).

Table 4. MDRO Healthcare-Associated Exposure Burden Metrics among *Escherichia coli* in the MHS, CY 2016

	Overall MDRO Prevalence[a]		Admission MDRO Prevalence[b]	
	Count	Rate[c]	Count	Rate[c]
Region				
OCONUS	192	11.0	181	10.4
US Midwest	150	15.4	147	15.1
US Northeast	3	--	3	--
US South	790	14.0	747	13.2
US South Atlantic	715	8.9	663	8.3
US West	847	11.4	804	10.8
Total	2,697	11.2	2,545	10.6

[a] Overall MDRO prevalence included all individuals with an MDRO infection identified from a sample collected at any point during the admission, as well as samples that tested positive for infection in the prior calendar year.
[b] Admission MDRO prevalence included all individuals with an MDRO infection identified from samples collected up to and including the third day of admission, as well as samples that tested positive for infection in the prior calendar year.
[c] Rates are presented as the rate per 1,000 inpatient admissions per year. Rates are not provided when the prevalence count is less than or equal to 10.
Data Source: NMCPHC HL7-formatted CHCS microbiology and Standard Inpatient Data Record (SIDR) databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Regional Epidemiologic Infection Classifications

Among all prevalent *E. coli* infections identified in the MHS during 2016, 85% were community-associated (CA) cases and 15% were healthcare-associated (HA) cases. Regionally, the proportion of HA cases ranged from 2.4% in the US Northeast to 17.6% in the US South (Figure 2).

HA cases were further categorized into hospital-onset (HO), community-onset (CO), or previous hospitalization (PH) groupings. Among all prevalent *E.coli* infections (regardless of HA or CA classification), the greatest proportion were classified as PH cases (9.7%), indicating that the *E. coli* infections were not associated with a current admission but the patient had a prior hospitalization in the previous 12 months. The second largest proportion of prevalent infections were CO cases (4.6%), indicating that the specimens were collected within the first three days of hospital admission and the infection most likely originated from the community. Only 0.7% of prevalent *E. coli* infections were HO cases, indicating the infection was identified after the third day of admission and likely contracted during the current hospitalization (data not shown). A similar distribution of HA case classifications were observed by region, where PH cases accounted for the largest percent, followed by CO cases and HO cases (Figure 2).

Figure 2. Proportion of Healthcare- and Community-Associated Cases among *Escherichia coli* Infection in the MHS by Region, CY 2016
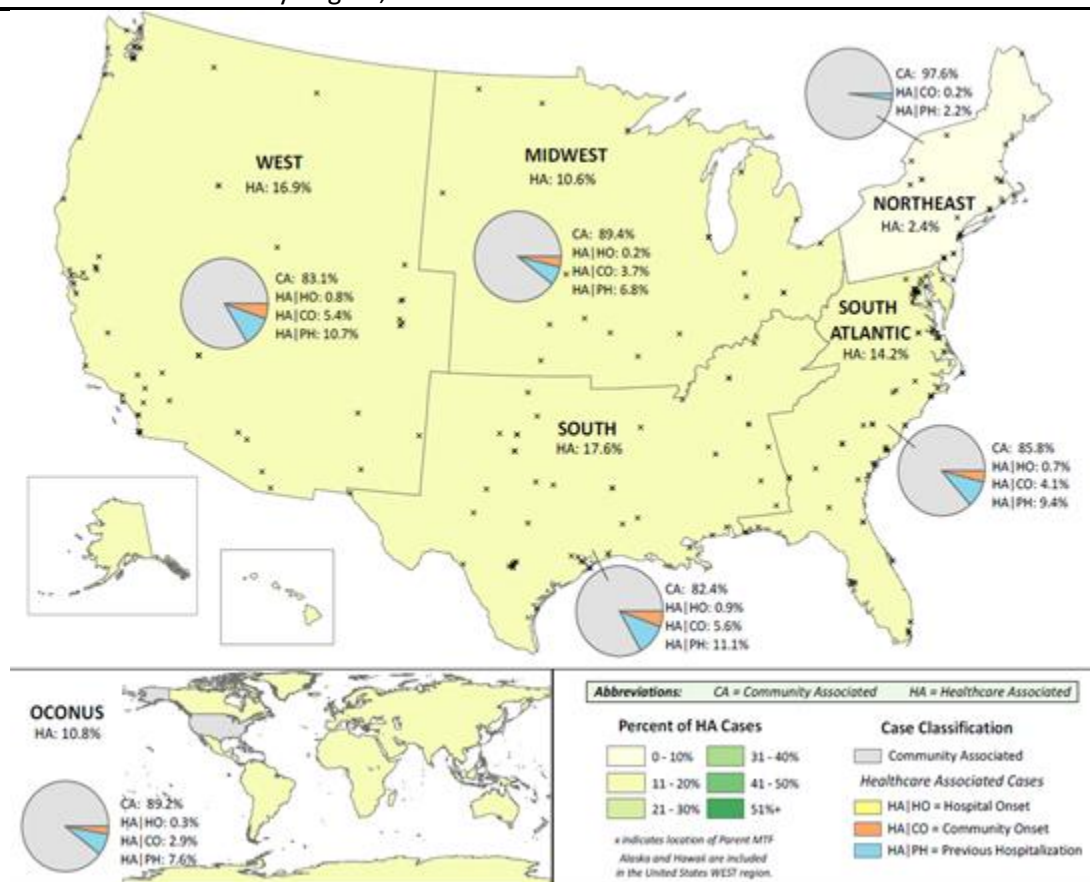
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Section B – Antimicrobial Resistance and Use
### Regional Multidrug Resistance

In 2016, the IR of *E. coli* was 676.7 infections per 100,000 persons per year; the IR of drug-resistant *E. coli* (i.e., resistant to antibiotics in at least three classes) was 122.8 infections per 100,000 persons per year. Regionally, locations outside the continental United States (OCONUS), as a group, had the highest total incidence rate of *E. coli* infections (1,125.4 per 100,000 persons per year). In the US, the total incidence rate of *E. coli* infections ranged from 152.4 per 100,000 persons per year in the Northeast to 794.4 per 100,000 persons per year in the West (Figure 3).

Approximately 21% of all prevalent *E. coli* infections were drug-resistant [(MDR), extensively drug-resistant (XDR), or possible extensively drug-resistant (PXDR)]. Of these prevalent infections, the majority were MDR (18.9%) and 1.7% were PXDR. There were no XDR infections identified among MHS beneficiaries in 2016. By region, the US South and US West demonstrated the largest percent of *E. coli* infections classified as PXDR, at 2.2% and 2.1%, respectively (Figure 3).

Prevalent *E. coli* infections were also assessed for carbapenem resistance (CR). CR *E. coli* infections accounted for 0.03% (n=22) of prevalent infections, which were distributed across the US South (n=6), US Midwest (n=6), US West (n=5), and US South Atlantic (n=5) regions.

Figure 3. Annual Incidence Rate (IR) and Percentage of Multidrug Resistance among *Escherichia coli* Infections in the MHS by Region, CY 2016
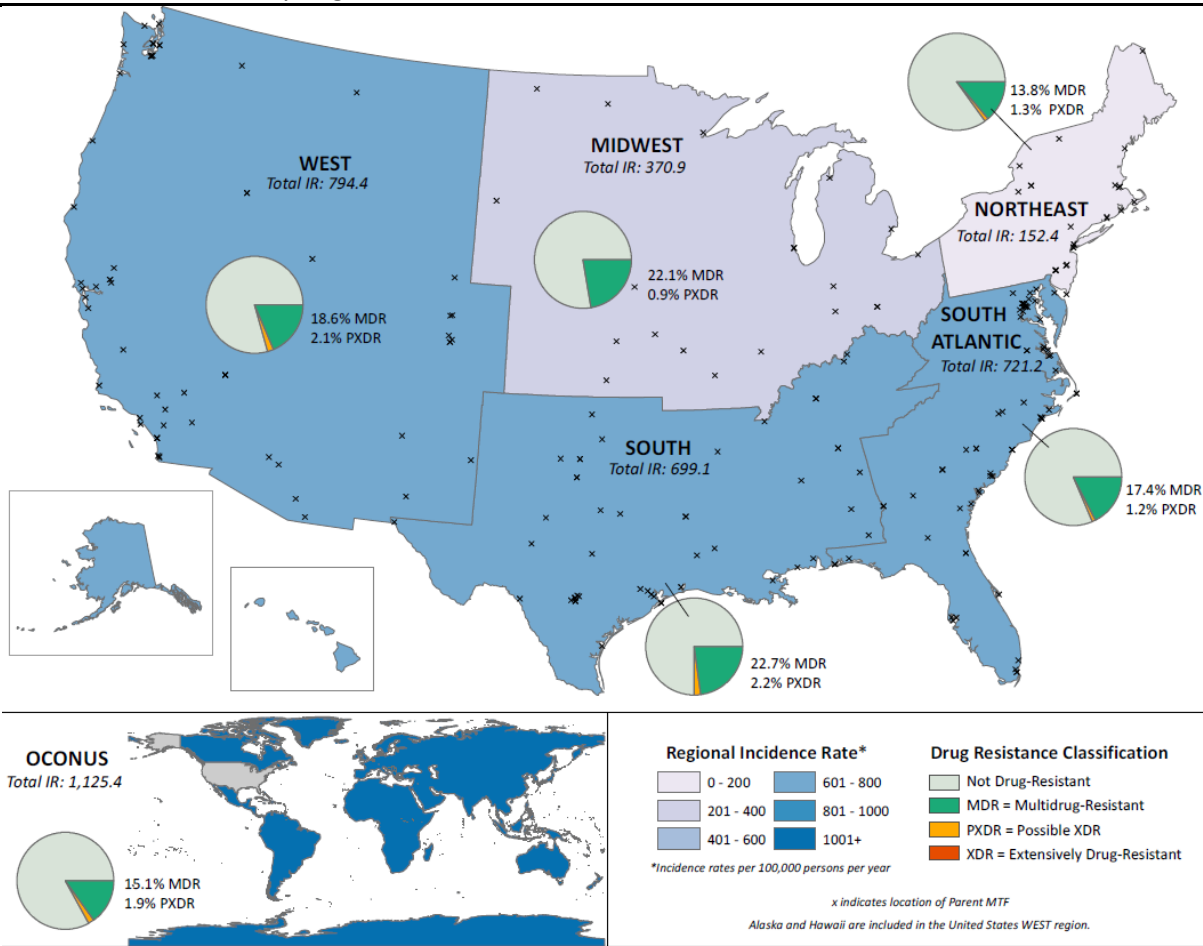
Rates are presented as the rate per 100,000 persons per year.
Data Source: NMCPHC HL7-formatted CHCS microbiology, SIDR, and MHS M2 databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Antibiogram

Table 5 displays an antibiogram of *E. coli* incident infections for all MHS beneficiaries from 2011 to 2016. In 2016, *E. coli* was most susceptible to carbapenems, including ertapenem (99.9%), imipenem (99.9%), and meropenem (99.9%). *E. coli* was least susceptible to ampicillin (61.2%) and ampicillin/sulbactam (63.0%). Statistically significant decreases in susceptibility from 2011 to 2016 were observed among 12 of the 21 drugs commonly used to treat *E. coli* infections. Four antibiotics demonstrated significant increases in susceptibility during the same time period, though the increasing trends were minimal; these antibiotics included amoxicillin/clavulanate, ampicillin, nitrofurantoin, and trimethoprim/sulfamethoxazole.

Table 5. Antibiogram of *Escherichia coli* Infections Identified in the MHS, CY 2011-2016

Antibiotics	2011	2012	2013	2014	2015	2016	Susceptibility Trend	Comment[a]
Amoxicillin/Clavulanate	88.0	86.9	87.3	87.5	88.0	88.2		↑
Ampicillin	61.2	60.5	61.1	61.4	61.6	61.2		↑
Ampicillin/Sulbactam	68.2	67.6	65.3	64.2	63.9	63.0		↓
Cefazolin	91.9	92.6	91.7	91.4	91.0	90.0		↓
Cefepime	98.1	98.2	98.0	98.1	97.6	97.6		↓
Cefotaxime	98.5	98.6	98.5	98.3	98.3	97.6		↓
Ceftazidime	98.0	97.9	97.7	97.8	97.5	97.5		↓
Ceftriaxone	97.5	97.7	97.3	97.2	96.8	96.7		↓
Cefuroxime	95.3	95.7	95.2	95.2	94.6	94.5		↓
Ciprofloxacin	90.9	90.6	90.3	90.2	89.9	89.3		↓
Ertapenem	99.9	99.9	99.9	99.9	99.9	99.9		
Gentamicin	94.7	94.6	94.5	94.4	94.3	94.2		↓
Imipenem	99.9	99.9	99.9	99.9	99.9	99.9		
Levofloxacin	91.5	91.3	90.8	90.3	90.1	89.5		↓
Meropenem	100.0	99.9	100.0	100.0	100.0	99.9		
Moxifloxacin	90.0	91.5	92.3	90.9	90.7	88.8		
Nitrofurantoin	97.4	96.4	96.4	96.1	97.0	97.9		↑
Piperacillin/Tazobactam	98.3	98.3	97.7	97.8	97.8	97.9		↓
Ticarcillin/Clavulanate	93.9	92.5	91.5	92.4	92.4	93.3		
Tobramycin	95.0	95.2	94.8	94.5	94.6	94.4		↓
Trimethoprim/Sulfamethoxazole	81.5	81.3	81.6	82.0	81.8	81.9		↑

'--' indicates that fewer than 30 isolates were tested.

[a] Arrow indicates the antibiotics with a significant change in direction of trend for significant two-tailed Cochrane-Armitage tests for trend established for a single antibiotic over time. A significant increase in susceptibility is denoted by a green upward arrow and a significant decrease in susceptibility is denoted by a blue downward arrow.

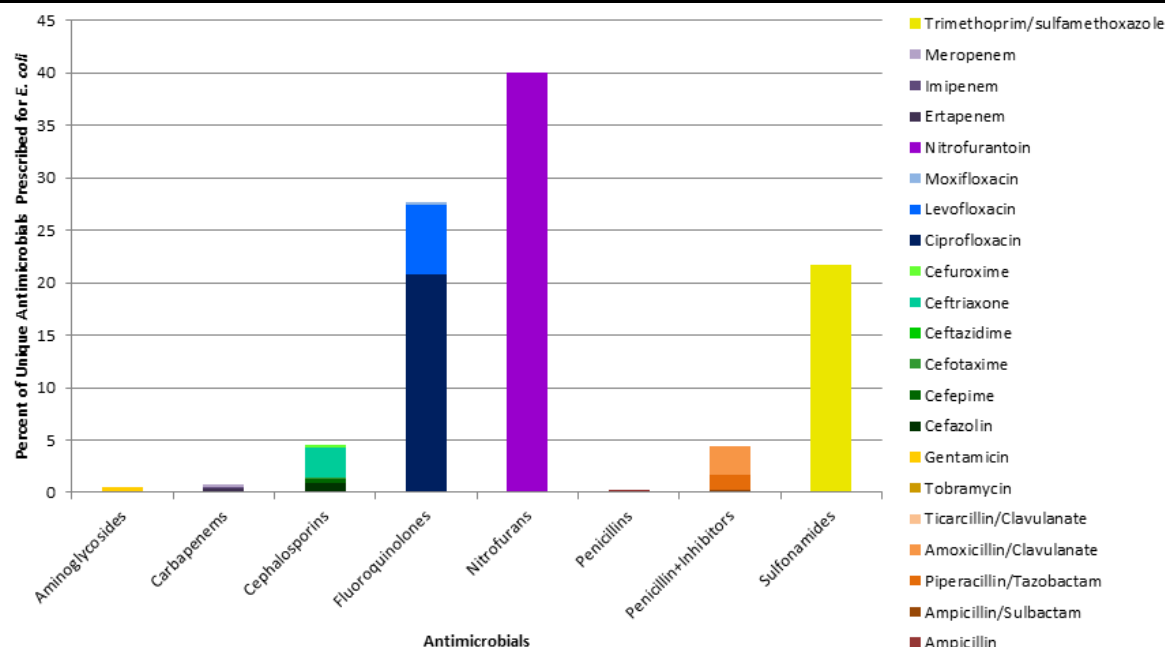Data Source: NMCPHC HL7-formatted CHCS microbiology database.

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Antimicrobial Consumption/Prescription Practices

Among all MHS beneficiaries, the most commonly prescribed antibiotic classes associated with *E. coli* infections in 2016 were nitrofurans (40.1%), followed by fluoroquinolones (27.7%) and sulfonamides (21.7%) (Figure 4). The most commonly administered antibiotic was nitrofurantoin (40.1%), followed by trimethoprim/sulfamethoxazole (21.7%), ciprofloxacin (20.7%), and levofloxacin (6.7%).

Figure 4. *Escherichia coli* Infection and Prescription Practices in the MHS, CY 2016

Only the first occurrence of a unique antibiotic was counted per person per infection, regardless of administration route.
Data Source: NMCPHC HL7-formatted CHCS microbiology and pharmacy databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Section C – Special Populations

Of the 65,535 prevalent *E. coli* infections in the MHS in 2016, 0.2% (n = 131) were Department of the Navy (DON) AD deployed personnel. Of these deployment-related infections, *E. coli* occurred with greatest frequency among females (91.6%) and personnel 18 to 24 years old (58.8%) (Table 6).

Table 6. Characteristics of DON AD Deployed Personnel with Deployment-Related *Escherichia coli* Infections in the MHS, CY 2016

	N = 131	
	Count	Percent
Deployed Personnel		
Gender		
Female	120	91.6
Male	11	8.4
Age Group (in Years)		
0-17	0	--
18-24	77	58.8
25-34	40	30.5
35-44	12	9.2
45-64	2	1.5
65+	0	--

Percent is presented as the percent of special population infections among all *E. coli* prevalence infections in CY 2016.
Data Source: NMCPHC HL7-formatted CHCS microbiology and CTS databases.
Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Discussion

The 2016 *E. coli* IR among all MHS beneficiaries remained relatively stable, just 3.1% above the weighted historic IR from 2013-2015. Service-specific and DOD AD rates all remained within two standard deviations of their respective historic IRs. Monthly IR trends exceeded weighted historic IR during the first two months of the year, which may be due in part to the *E. coli* incident infection definition. Only the first occurrence of an *E. coli* infection was counted per person per year; if a person had multiple episodes of an *E. coli* infection throughout the year (e.g., a recurrent *E. coli* UTI), the first would be counted once at the beginning of the year, resulting in seemingly inflated IRs early in the calendar year. Seasonal rates and variability cannot be corroborated by the literature, which has yet to determine a direct seasonal correlation due to the variety of illnesses and mechanisms through which *E. coli* causes disease.[4]

Evaluation of clinical and demographic characteristics found the *E. coli* IR in females was 11 times higher than males, and the majority of prevalent infections clinically manifested as UTIs (96%). These results are consistent with literature describing UTIs caused by *E. coli* as one of the most common extraintestinal infections among young, otherwise healthy, sexually active women.[5] Screening practices may also contribute to higher rates of *E. coli* infections among females of reproductive age, as the Infectious Disease Society of America and US Preventive Services Task Force recommend screening for asymptomatic bacteriuria among pregnant women and those undergoing urological procedures.[6,7] Existing literature describing *E. coli* as the primary etiological agent for CA UTIs in the general US population also aligns with results demonstrated from this assessment, describing the majority of prevalent *E. coli* infections among MHS beneficiaries as CA (85%).[5,8]

Resistant *E. coli* infections pose serious challenges to clinical treatment and can reduce mission readiness.[9-12] Assessments of CR *E. coli* infections demonstrate variable but low annual frequencies over the past three years; a total of 24 infections were identified in 2015, followed by 14 infections in 2014, and 25 infections in 2013.[1] Almost 19% of all prevalent *E. coli* infections in MHS beneficiaries were classified as MDR in 2016, indicating the infection had specimens non-susceptible to at least one antibiotic from at least three different antibiotic classes. This finding is similar to estimates reported for the general US population; one study assessing over 30,000 outpatient urinary *E. coli* isolates from The Surveillance Network (TSN) Database USA during 2010 found 17% met the MDR definition, demonstrating resistance to three or more tested antimicrobial agents.[13] The current assessment found regions with the highest total IRs and analyses defining MDRO healthcare-associated exposure burden metrics implicate high levels of importation of drug-resistant *E. coli* from the community to healthcare settings within each region. The admissions MDRO prevalence rate during 2016 (10.6 per 1,000 inpatient admissions) accounted for approximately 94% of the overall MDRO prevalence metric (11.2 per 1,000 inpatient admissions), demonstrating the majority of MDRO burden for *E. coli* were identified within the first three days of an inpatient admission and thus more likely community-onset rather than a result of the hospital setting. These results underscore the need for drug-resistance surveillance outside of hospital settings.

E. coli infections retained high susceptibilities to several antibiotics, indicating a range of viable treatment options. Nitrofurantoin, a first-line antibiotic recommended for uncomplicated UTIs in non-seriously ill patients,[14,15] was the most commonly prescribed treatment (40.1%) identified among MHS beneficiaries with *E. coli* infections in 2016. Antibiogram results support these treatment practices, as nitrofurantoin susceptibility increased significantly to 97.9% in 2016. Trimethoprim/sulfamethoxazole (21.7%) and ciprofloxacin (20.7%) were the second and third most commonly prescribed antibiotics for *E. coli* infections during 2016, but, as of the most recently published Johns Hopkins Antibiotic Guide, neither are preferred treatments for UTIs caused by *E. coli*.[15] The Johns Hopkins Antibiotic Guide indicates use of trimethoprim/sulfamethoxazole for UTIs only when expected resistance rates are less than 20%; however, antibiogram results for this particular antibiotic during 2016 indicate resistance patterns among MHS beneficiaries nearly exceed this cutoff (18.1%).[15] Additionally, the recent increase in *E. coli* fluoroquinolone resistance has been demonstrated in relation to increased prescribing practices, both in civilian and military cohorts.[14,16] An assessment among DOD beneficiaries noted a moderate positive correlation between ciprofloxacin prescriptions and ciprofloxacin resistance for *E. coli* isolates from inpatient settings between 2010 and 2014.[16] The current analysis identified a statistically significant decrease for ciprofloxacin susceptibility among *E. coli* infections, from 90.9% in 2011 to 89.3% in 2016.

In summary, this report documents a minor upward trend in *E. coli* infection rates among MHS beneficiaries in relation to the 2013-2015 weighted historic IR. However, in contrast to the MHS *E. coli* infection rates from 2015 alone (702.3 per 1000,000 person years), the 2016 *E. coli* infection rate (676.6 per 100,000 person years) may signal a stabilization, or the beginning of a declining trend should rates continue to decrease in 2017. The characteristics of *E. coli* infections in 2016 are concurrent with existing literature reporting elevated rates among females, clinical presentation as UTIs, and a preponderance of CA cases. The large proportion of drug-resistant *E. coli* infections identified during 2016, along with elevated MDRO admission prevalence rates, underscore the need for surveillance outside of hospital settings. Finally, analysis of antibiotic susceptibility patterns indicate that viable treatment options are present for *E. coli* infections; however, the declining susceptibility of ciprofloxacin, in combination with resistance patterns from the general US population, merit further attention. Continued surveillance for *E. coli* is warranted to monitor any changes in burden, susceptibility, and treatment options and to guide targeted prevention efforts.

References

1. Hudson TM, Chukwuma U. Annual Surveillance Summary: *Escherichia coli* (E. coli) Infections in the Military Health System (MHS), 2015. EpiData Center at the Navy and Marine Corps Public Health Center web site. http://www.med.navy.mil/sites/nmcphc/Documents/epi-data-center/Annual_Report_2015_ECOLI_FINAL.pdf. Published March 2017. Accessed 24 May 2017.

2. EpiData Center at the Navy and Marine Corps Public Health Center. 2015 Surveillance Summaries: Bacterial Infections in the Military Health System (MHS). http://www.med.navy.mil/sites/nmcphc/epi-data-center/Pages/2015-surveillance-summaries.aspx. Published March 2017. Accessed 31 May 2017.

3. EpiData Center at the Navy and Marine Corps Public Health Center. 2016 Surveillance Summaries: Bacterial Infections in the Military Health System (MHS). http://www.med.navy.mil/sites/nmcphc/epi-data-center/Pages/2016-surveillance-summaries.aspx. Published June 2017. Accessed 30 June 2017.

4. Freeman JT, Anderson DJ, Sexton DJ. Seasonal peaks in *Escherichia coli* infections: possible explanations and implications. *Clin Microbiol Infect*. 2009;15(10): 951-3.

5. Manges AR, Tabor H, Tellis P, et al.. Endemic and epidemic lineages of *Escherichia coli* that cause urinary tract infections. *Emerg Infect Diseases*. 2008;10(14):1575-1583.

6. Lin K, Fajardo K. Screening for asymptomatic bacteriuria in adults: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med.* 2008;149:W20-W24.

7. Nicolle LE, Bradley S, Colgan R, et al. Infectious Disease Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infec Dis*. 2005;40:643-54.

8. Vincent C, Boerlin P, Daignault D, et al. Food reservoir for *Escherichia coli* causing urinary tract infections. *Emerg Infect Diseases*. 2010;1(16):88-95.

9. Aronson NE, Sanders JW, Moran KA. In harm's way: infections in deployed American military forces. *Clin Infect Dis*. 2006;43:1045-1051.

10. Abdul Rahaman Shariff VA, Suchitra Shenoy M, et al. The antibiotic susceptibility patterns of uropathogenic *Escherichia coli*, with special reference to the fluoroquinolones. *J Clin Diagn Res*. 2013;7(6):1027-1030.

11. Karlowsky JA, Lagacé-Wiens PRS, Simner PJ, et al. Antimicrobial resistance in urinary tract pathogens in Canada from 2007-2009: CANWARD surveillance study. *Antimicrob Agents Chemother.* 2011;55(7):3169-3175.

12. Levison ME, Kaye D. Treatment of complicated urinary tract infections with an emphasis on drug-resistant gram-negative uropathogens. *Curr Infect Dis Rep.* 2013;15:109-115.

13. Sanchez GV, Baird AMG, Karlowsky JA, et al. Nitrofurantoin retains antimicrobial activity against multidrug-resistant urinary *Escherichia coli* from US outpatients. *J Antimicrob Chemother.* 2014;69(12):3259-3262.

14. Shepherd AK, Pottinger PS. Management of urinary tract infections in the era of increasing antimicrobial resistance. *Med Clin North Am.* 2013;97(4):737-57, xii.

15. Auwaerter P. *Escherichia coli*. Johns Hopkins Antibiotic (ABX) Guide. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540214/all/ Escherichia_coli. Updated 06 April 2017. Accessed 26 May 2017.

16. Spencer JR, Milburn EK, Chukwuma, U. Correlation between antimicrobial resistance in *Escherichia coli* infections in hospitalized patients and rates of inpatient prescriptions for selected antimicrobial agents, Department of Defense hospitals, 2010–2014. *Medical Surveillance Monthly Report*. 2016;23(3):6-10.

Appendix A: Antibiotics Used to Identify Resistance among *Escherichia coli* Infections in the MHS, CY 2016

Table A-1. Antibiotics Used to Identify Resistance among *Escherichia coli* Infections in the MHS, CY 2016

Antibiotic Class	Antibiotics Included in Class
Aminoglycosides	Amikacin
	Gentamicin
	Tobramycin
Antipseudomonals penicillins & β-lactamase inhibitors	Piperacillin/Tazobactam
	Ticarcillin/Clavulanic Acid
Carbapenems	Ertapenem
	Imipenem
	Meropenem
1st and 2nd Generation Cephalosporins (non-extended spectrum cephalosporins)	Cefazolin
	Cefuroxime
3rd and 4th Generation Cephalosporins (extended spectrum cephalosporins)	Cefotaxime
	Ceftriaxone
	Ceftazidime
	Cefepime
Fluoroquinolones	Moxifloxacin
	Ciprofloxacin
	Levofloxacin
Nitrofurans	Nitrofurantoin
Sulfonamides	Trimethoprim/Sulfamethoxazole
Penicillins	Ampicillin
Penicillins & β-lactamase inhibitors	Amoxicillin/Clavulanic Acid
	Ampicillin/Sulbactam

Prepared by the EpiData Center Department, Navy and Marine Corps Public Health Center, on 21 June 2017.

Appendix B: Acronym and Abbreviation List

Acronym/Abbreviation	Definition
AD	active duty
CA	community-associated
CHCS	Composite Health Care System
CO	community-onset
CONUS	continental United States
CR	carbapenem-resistant
CTS	Contingency Tracking System
CY	calendar year
DMDC	Defense Manpower Data Center
DOD	Department of Defense
DON	Department of the Navy
EDC	EpiData Center Department
HA	healthcare-associated
HL7	Health Level 7 format
HO	hospital-onset
IR	incidence rate
M2	MHS Data Mart
MDR	multidrug-resistant
MDRO	multidrug-resistant organism
MHS	Military Health System
MTF	military treatment facility
NMCPHC	Navy and Marine Corps Public Health Center
OCONUS	outside the continental United States
PXDR	possible extensively drug-resistant
PH	previous hospitalization
SIDR	Standard Inpatient Data Record
TSN	The Surveillance Network (TSN) Database USA
US	United States
UTI	urinary tract infection
XDR	extensively drug-resistant